

WHAT IS CLAIMED IS:

1. , A method of enhancing pericyte cell proliferation comprising administering to a subject in need thereof an amount of a BPI protein product effective to enhance proliferation of pericyte cells.

5            2.        The method of claim 1 wherein the onset of diabetic retinopathy is prevented.

10            3.        The method of claim 1 wherein the subject is suffering from a complication of diabetes selected from the group consisting of diabetic polyneuropathy, diabetic nephropathy, skeletal muscle degeneration after pericyte degeneration, and other organ complications of diabetes.

15            4.        The method of claim 1 wherein the subject is suffering from a disease associated with the presence of autoantibodies to pericytes.

20            5.        The method of claim 1 wherein the subject is suffering from age-related macular degeneration (ARMD).

25            6.        The method of claim 1 wherein the subject is suffering from ovarian failure.

7.        The method of claim 1 wherein the subject is suffering from multiple sclerosis.

25            8.        The method of claim 1 wherein the subject is suffering from Alzheimer's disease, or traumatic brain injury, or other conditions involving perturbation of the blood-brain-barrier, or partial seizures.

9. The method of claim 1 wherein the subject is pregnant and  
placental development is enhanced.

10. The method of claim 1 wherein the subject is in need of wound  
healing, and the BPI protein product is administered in an amount and under  
5 conditions effective to enhance production of fibroblasts.

11. The method of claim 1 wherein the subject is suffering from a  
bone degenerative disorder, and the BPI protein product is administered in an amount  
and under conditions effective to enhance production of chondroblasts or osteoblasts.

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12. A method of inhibiting pericyte cell proliferation comprising  
administering to a subject in need thereof an effective amount of an agent that inhibits  
BPI protein product-induced proliferation of pericyte cells.

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13. The method of claim 12 wherein the subject is suffering from  
hypertension.

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14. The method of claim 12 wherein the subject is suffering from a  
disorder associated with vascular disease selected from the group consisting of  
formation of vascular calcifications and atherosclerotic plaques, atherosclerosis,  
restenosis, cerebrovascular ischemia, stroke, coronary artery disease, myocardial  
ischemia, myocardial infarction, peripheral vascular disease, Raynaud's syndrome,  
early occlusion of peripheral arteries and vascular remodeling associated with  
pulmonary hypertension.

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15. The method of claim 12 wherein the subject is suffering from  
acute respiratory distress syndrome (ARDS).

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16. The method of claim 12 wherein the subject is suffering from  
endometriosis or adenomyosis.

17. ✓ A method of enhancing retinal epithelial cell proliferation comprising administering to a subject in need thereof an amount of a BPI protein product effective to enhance proliferation of retinal epithelial cells.

5                18.      The method of claim 17 wherein the subject is suffering from retinitis pigmentosa.

10                19.      The method of claim 17 wherein the subject is suffering from age-related macular degeneration.

15                20.      The method of claim 1 wherein the BPI protein product is an amino-terminal fragment of BPI protein having a molecular weight of about 20 kD to 25 kD, or a dimeric form thereof.

20                21.      The method of claim 1 wherein the BPI protein product is a BPI-derived peptide.

25                22.      The method of claim 21 wherein the BPI-derived peptide is XMP.679.

30                23.      A method of screening for a candidate inhibitor of BPI-induced proliferation of pericytes comprising the steps of:

                      (a)     detecting proliferation of pericytes in the presence of BPI protein product and in the presence and absence of a test compound; and

                      (b)     identifying said test compound as a candidate inhibitor of BPI-induced proliferation when proliferation of the pericytes is reduced in the presence of the test compound.

24. *j* A method of screening a BPI protein product for the ability to enhance proliferation of pericytes comprising the steps of:

- (a) detecting proliferation of pericytes in the presence and absence of a BPI protein product; and
- 5 (b) identifying a BPI protein product as a candidate enhancer of pericyte proliferation when proliferation of the pericytes is increased in the presence of the BPI protein product.

25. *j* A method of screening for a candidate enhancer of pericyte proliferation comprising the steps of:

- 10 (a) measuring proliferation of pericytes in the presence and absence of a test compound;
- (b) measuring proliferation of pericytes in the presence of said test compound and a BPI protein product, said BPI protein product at a concentration effective to enhance pericyte proliferation; and
- 15 (c) identifying said test compound as a candidate enhancer of pericyte proliferation when pericyte proliferation is increased in step (a) but not further increased in step (b).

20 26. *i* A method of screening for a candidate enhancer of pericyte proliferation comprising the steps of:

- (a) measuring proliferation of pericytes in the presence and absence of a test compound;
- 25 (b) measuring proliferation of pericytes in the presence of said test compound and a BPI protein product, said BPI protein product at a concentration effective to enhance pericyte proliferation; and
- (c) identifying said test compound as a candidate enhancer of pericyte proliferation when the increase in pericyte proliferation measured in step (a) is about the same as or less than the increase in pericyte proliferation measured in step (b).

27. A method of enhancing epithelial cell proliferation comprising administering to a subject in need thereof an amount of a BPI protein product effective to enhance proliferation of epithelial cells.

5 28. The method of claim 27 wherein the subject is suffering from retinitis pigmentosa or age-related macular degeneration.

29. A method of screening for a candidate inhibitor of BPI-induced proliferation of epithelial cells comprising the steps of:

10 (a) detecting proliferation of epithelial cells in the presence of BPI protein product and in the presence and absence of a test compound; and

(b) identifying said test compound as a candidate inhibitor of BPI-induced proliferation when proliferation of the epithelial cells is reduced in the presence of the test compound.

15 30. A method of screening a BPI protein product for the ability to enhance proliferation of epithelial cells comprising the steps of:

(a) detecting proliferation of epithelial cells in the presence and absence of a BPI protein product; and

20 (b) identifying a BPI protein product as a candidate enhancer of epithelial cell proliferation when proliferation of the epithelial cells is increased in the presence of the BPI protein product.

25 31. A method of screening for a candidate enhancer of epithelial cell proliferation comprising the steps of:

(a) measuring proliferation of epithelial cells in the presence and absence of a test compound;

(b) measuring proliferation of epithelial cells in the presence of said test compound and a BPI protein product, said BPI protein product at a concentration effective to enhance epithelial cell proliferation; and

(c) identifying said test compound as a candidate enhancer of epithelial cell proliferation when epithelial cell proliferation is increased in step (a) but not further increased in step (b).

5               32. The method of any one of claims 23, 24, 25, 26, 29, 30 or 31 wherein proliferation is determined by the measuring the amount of MAP kinase phosphorylation.

10              33. A method of enhancing pericyte proliferation in a subject with diabetes-induced retinal vascular permeability comprising administering to the subject an amount of a BPI protein product effective to enhance proliferation of pericytes.

15              34. The method of claim 33 wherein the diabetes-induced retinal vascular permeability is reduced.

20              35. A method of enhancing pericyte proliferation in a subject suffering from a pericyte degeneration disorder that is complications of diabetes, diseases associated with the presence of autoantibodies to pericytes, age-related macular degeneration (ARMD), ovarian failure, multiple sclerosis, Alzheimer's disease, traumatic brain injury, a condition involving perturbation of the blood-brain-barrier, partial seizures, or and placental development in pregnancy, comprising administering to the subject an amount of a BPI protein product effective to enhance proliferation of pericytes.

25              36. A method of enhancing cell proliferation in a subject in need of wound healing, comprising administering to the subject an amount of a BPI protein product effective to enhance production of fibroblasts cells.

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37. / A method of enhancing cell proliferation in a subject suffering from a bone degenerative disorder, comprising administering to the subject an amount of a BPI protein product effective to enhance production of chondroblasts or osteoblasts.

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38. / A method for reducing pericyte proliferation in a subject suffering from a condition where pericyte proliferation is deleterious, that is hypertension, vascular calcifications, atherosclerotic plaques, atherosclerosis, restenosis, cerebrovascular ischemia, stroke, coronary artery disease, myocardial ischemia, myocardial infarction, peripheral vascular disease, Raynaud's syndrome, early occlusion of peripheral arteries and vascular remodeling associated with pulmonary hypertension, acute respiratory distress syndrome (ARDS), endometriosis or adenomyosis, comprising administering to the subject an amount of an agent that inhibits BPI protein product-induced proliferation of pericyte cells.

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39. / A method for enhancing cell proliferation in a subject suffering from a retinal epithelial degeneration disorder that is retinitis pigmentosa or age-related macular degeneration, comprising administering to the subject an amount of a BPI protein product effective to enhance proliferation of retinal epithelial cells.

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